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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,632	01/14/2004	Bianca Baroli	0492611-0520	4661

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EXAMINER	
BARNHART, LORA ELIZABETH	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
12/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@choate.com

Office Action Summary	Application No.	Applicant(s)	
	10/757,632	BAROLI ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6,12,21,22,25-31,56,57 and 82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6,12,21,22,25-31,56,57 and 82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments

Applicant's amendments filed 10/3/08 to claims 1, 3, 21, 29-31, and 56 have been entered. Claims 83 and 84 have been cancelled in this reply. No claims have been added. Claims 1, 3, 6, 12, 21, 22, 25-31, 56, 57, and 82 remain pending in the current application, all of which are being considered on their merits. References not included with this Office action can be found in a prior action. Any rejections of record not particularly addressed below are withdrawn in light of the claim amendments and applicant's comments.

Election/Restrictions

Applicant's election with traverse of the species "tissue engineering," "gelatin," "protein," "sugar," "polyethylene glycol," "cross-linked synthetic polymer," "granulation," "visible radiation," and "dissolution-controlled systems" in the reply filed on 4/23/07 is still in effect over the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 6, 12, 21, 22, 25-31, 56, 57, and 82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are interpreted as being drawn to a composition comprising three components in a mixture: (a) a photo-polymerized cross-linked polymer; (b) bioactive molecules; and (c) a material insoluble by the polymer (“insoluble material”). The claims require that the insoluble material both protect the bioactive molecules from the degradation that would be caused by photo-polymerization and transitions from a solid to a gel when it is placed at or above the approximate body temperature of an organism. It is this insoluble material that is the primary subject of this rejection.

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co.*, Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179

(Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). See M.P.E.P. § 2163.02. In this case, the skilled artisan would not have reasonably concluded at the time of the invention that applicant was in possession of the entire invention as claimed.

M.P.E.P. §2163 recites, "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus…when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. **For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.**"

In this case, the "insoluble material" is described (with the exception of claim 6) using functional language, and the specification does not provide sufficient description that the skilled artisan would have concluded at the time of the invention that applicant

was in possession of each and every “insoluble material” with the recited properties. At page 4, lines 22-23, the specification provides a few examples of insoluble materials: “gelatin, collagen, natural polymer, or synthetic polymer.” However, this list includes literally millions of possible compounds (e.g., every protein is a “natural polymer"), and the specification includes no criteria for identifying which of these candidate “insoluble materials” have the recited properties. The exemplary list provided in the specification is broad and diverse, including widely variant species. The working examples appear to make use of only one insoluble material, gelatin (page 8, line 15, e.g.) and therefore do not assist in providing the necessary criteria by which skilled artisan could immediately envisage those compounds that can act as the “insoluble material” and which are not.

Furthermore, according to claim 1, the term “insoluble material" depends completely on the structure of the selected polymer. The specification teaches that gelatin is insoluble in monomers of PEGDM (polyethylene glycol-dimethacrylate; page 7, line 28, and page 18, line 18). Again, however, the specification provides no guidance (other than implied trial-and-error) for determining whether a candidate insoluble material would be insoluble in a selected polymer, especially given that the specification appears to be wholly silent on the solubility of the exemplified insoluble material, gelatin, in the exemplified polymer, polymerized PEGDM (the specification comments only on the solubility of gelatin in monomeric PEGDM).

Finally, the specification provides no guidance (other than implied trial-and-error) for identifying the protective effect of a given insoluble material on a given bioactive molecule. The working examples illustrate an effect on a few enzymes by one insoluble

material, gelatin, in a composition comprising PEGDM polymerized by ethyl 4-dimethylaminobenzoate (EDMAB) and camphorquinone (CQ) (see page 7, lines 26-27, and page 8, line 5, through page 9, line 20). The specification does not consider whether gelatin is protective against any photopolymerization initiators other than EDMAB and CQ and provides no criteria for making such a determination other than implied trial-and-error.

In short, claim 1 and its dependents attempt to describe a composition using functional language almost exclusively, but the specification includes only one example of a combination of components that interact with each other as claimed and provides no guidance for identifying additional combinations that would meet the limitations of the claims. The skilled artisan would not immediately envisage each and every combination of components with the recited properties; therefore, written description is lacking.

Claim 3 remains rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition that repairs or restructures tissue when administered to an organism, does not reasonably provide enablement for a composition that replaces tissue per se. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the

state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

Claim 3 is drawn in part to a composition that may be "substituted for" tissue in an organism. Tissue, by definition, is a composition comprising an aggregate of cells and their supportive matrix (http://www.merriam-webster.com/dictionary/tissue). Therefore, a composition that could substitute for a tissue necessarily includes cells. Claim 1 does not include cells, and the specification does not appear to contemplate embodiments in which cells are placed into the instantly claimed composition. While a singular, narrow working embodiment cannot be a sole factor in determining enablement, its limited showing, in light of the unpredictable nature of the art and the lack of direction applicants present, provides additional weight to the lack of enablement in consideration of the *Wands* factors as a whole. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention across its entire scope.

It is noted that applicant has replaced the term "replace" with the term "substitute for," but the examiner submits that these terms are synonyms. The specification does not teach a cell-free construct that is a true "tissue substitute" in the full sense of the term.

Claims 1, 3, 6, 12, 21, 22, 25-31, 56, 57, and 82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Claim 1 is drawn to a composition that comprises a polymer and "a material insoluble by the polymer," but there appears to be no basis for this limitation in the specification. The specification addresses the solubility of the material in the monomers that go on to make the polymer, but it is silent as to the solubility of the insoluble material in the polymer itself. Because claims 3, 6, 12, 21, 22, 25-31, 56, 57, and 82 depend from unsupported claim 1, they must also be rejected under 35 U.S.C. 112, first paragraph.

Applicant's comments regarding the withdrawn art rejections have been considered to the extent they apply to the new rejections, but these comments do not appear to be pertinent to the points raised above that were necessitated by applicant's amendment.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 6, 12, 21, 22, 25-31, 56, 57, and 82 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

According to its broadest reasonable interpretation, claim 1 is drawn to a composition comprising three components in a mixture: (a) a photo-polymerized cross-linked polymer (i.e., this first component is already polymerized); (b) bioactive molecules; and (c) a material insoluble by the polymer ("insoluble material"). The claims require that the insoluble material both protect the bioactive molecules from the degradation that would be caused by some photo-polymerization conditions and transition from a solid to a gel when it is placed at or above the approximate body temperature of an organism. In other words, the claims appear to be drawn to a product that results from the photo-polymerization of photo-polymerizable monomers and that also contains bioactive molecules and an insoluble material and that, when placed at a particular temperature, desolidifies to form a gel. However, this interpretation (one which appears to be supported by applicant's arguments) raises issues under section 112, second paragraph.

Since component (a) is already photo-polymerized in this composition, it is not clear how the "photo-polymerizing environment" from which the insoluble material affords protection relates to the composition. The claim does not require that the insoluble material or bioactive molecules were present when the monomers constituting the photo-polymerized cross-linked polymer were photo-polymerized, so the protection does not necessarily relate to that step. All that the claim requires is a mixture of three

components: a polymer, a bioactive molecule, and an insoluble material. The relationships among the components are not clear; applicant appears to be implying a time element that is not distinctly pointed out in the claims. If applicant means to claim a composition containing the three recited components that results when a mixture of photo-polymerizable monomers, a bioactive molecule, and an insoluble material are placed into a photo-polymerizing environment, the claim should particularly recite such. Currently, claim 1 is drawn to a composition in which polymer, bioactive molecules, and insoluble material are simply mixed together.

Claim 1 requires that the insoluble material "shields the bioactive molecules from a polymerization process," but the nature and extent of this shielding is not clear, so the scope of the components that could perform the shielding is not clear. While features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus (or composition) must be distinguished from the prior art in terms of structure rather than function. *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997). The claims do not describe the "insoluble material" in any way other than by its function, and the specification does not appear to include criteria for determining which compounds are within the genus of "insoluble materials" and which are not. Since the metes and bounds of this term cannot be determined, the claim is indefinite. Clarification is required.

Because claims 3, 6, 12, 21, 22, 25-31, 56, 57, and 82 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Applicant alleges generally that photopolymerization processes can degrade enzymes and that the insoluble material prevents this degradation (Reply, page 6, paragraph 1). These arguments have been fully considered, but they are not persuasive. First, no claims are limited to compositions in which the biomolecules are enzymes, so the remarks are not commensurate in scope with the claim. More importantly, though, the remarks commit the same error as the claims in that they address the insoluble material only by what it does, but not what it is. The remarks do not shed light on the central issue, i.e. the structures of those components that could perform the recited function.

Claim 3 allows that the composition can be "substituted for" tissue in an organism. It is not clear how the composition of claim 1 as claimed can actually replace tissue, since there are no cells in the composition, and cells cannot reasonably be considered "bioactive molecules." Tissue necessarily includes cells. Clarification is required. This point has been discussed above in the enablement rejection.

Claim 31 requires that the photopolymerization means in claim 30 "polymerize the monomers with visible radiation." However, it is not clear whether the photopolymerization means is light itself or, rather, compounds that promote polymerization when they are exposed to light. The scope of the "photopolymerization means" is still not clear. Clarification is required. Applicant alleges generally that the claim is definite (Reply, page 7, paragraph 1), but the examiner disagrees for the reasons set forth above.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is (571)272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651